

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Boldogh et al. Group Art Unit: 1617
Serial No.: 10/691,330 Examiner: Unassigned
Filed: October 22, 2003 Docket No.: 265.00390101
Confirmation No.: 1384
Title: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF AS INHIBITORS OF APOPTOSIS AND OTHER CELLULAR DAMAGE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

We are transmitting the following documents along with this Transmittal Sheet (which is submitted in triplicate):

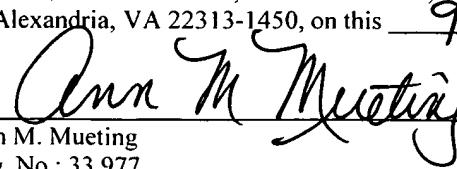
An itemized return postcard.
 A Petition for Extension of Time for month(s) and a check in the amount of \$ for the required fee.
 An Information Disclosure Statement (2 pgs); copies of 1 applications; 1449 forms (13 pgs); and copies of 147 documents cited on the 1449 forms.
 A check in the amount of \$, for .
 A certified copy of a application, Serial No. , filed , the right of priority of which is claimed under 35 U.S.C. §119.
 Other:
 Amendment No Additional fee is required. The fee has been calculated as shown:

Fee Calculation for Claims Pending After Amendment					
	Pending Claims after Amendment (1)	Claims Paid for Earlier (2)	Number of Additional Claims (1-2)	Cost per Additional Claim	Additional Fees Required
Total Claims				x \$18 =	
Independent Claims				x \$86 =	
One or More New Multiple Dependent Claims Presented? If Yes, Add \$290 Here →					
Total Additional Claim Fees Required					

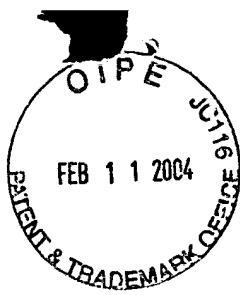
Please consider this a PETITION FOR EXTENSION OF TIME for a sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 13-4895. Triplicate copies of this sheet are enclosed.

CERTIFICATE UNDER 37 C.F.R. §1.8: The undersigned hereby certifies that this Transmittal Letter and the paper(s), as described hereinabove, are being deposited in the United States Postal Service, as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 9 day of February, 2004.

MUETING, RAASCH & GEBHARDT, P.A.
Customer Number: 26813

By: 
Ann M. Mueting
Reg. No.: 33,977
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Facsimile: 612-305-1228

(LARGE ENTITY TRANSMITTAL UNDER RULE 1.8)



PATENT
Docket No.265.00390101

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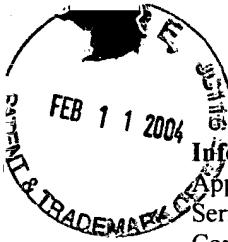
INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with C.F.R. §§ 1.97 *et. seq.*, the materials enclosed herewith are brought to the attention of the Examiner as possibly being of interest in connection with the above-identified patent application. Per M.P.E.P. § 609, the information cited in the present Information Disclosure Statement shall not be construed to be an admission that the information is, or is considered to be, material to patentability. Consideration of each of the documents listed on the attached 1449 form(s) is respectfully requested. As this patent application was filed after June 30, 2003, copies of the U.S. patents and U.S. patent application publications listed on the attached 1449 form(s) have not been submitted). Pursuant to the provisions of M.P.E.P. §609, Applicants further request that a copy of the 1449 form(s), marked as being considered and initialed by the Examiner, be returned with the next Official Communication.

Applicants also wish to bring the Examiner's attention to the following pending U.S. Applications, as well as any documents, Office Actions that may include rejections of similar claims, and any provisional U.S. patent applications referenced in the pending U.S. applications or in their file wrappers. A copy of each of the below-listed pending U.S. Patent Applications is provided herewith.

**Information Disclosure Statement**

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Page 2 of 2

List of Pending Non-Published U.S. Patent Applications

Applicant(s)	Application Number	Filing Date	Serial No. of Provisional Application to which listed Application claims priority
Boldogh et al.	10/691,157	October 22, 2003	60/420,369

It is believed that no fee is due, as this Information Disclosure Statement is filed prior to the receipt of any Action on the merits. However, in the event a fee is due, please charge any fee or credit any overpayment to Account No. 13-4895.

The Examiner is invited to contact Applicants' Representatives at the below-listed telephone number, if they can be of any assistance during prosecution of the present application.

Respectfully submitted for
Boldogh et al.

By
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CERTIFICATE UNDER 37 C.F.R. 1.8:	
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Name: Ann M. Muetting	

February 9, 2004
Date

By: Ann M. Muetting
Ann M. Muetting
Reg. No. 33,977
Direct Dial (612)305-1217

INFORMATION DISCLOSURE STATEMENT	
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U.S. PATENT & TRADEMARK OFFICE	

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Applicant(s): Boldogh et al.	Confirmation No.: 1384
Application Filing Date: October 22, 2003	Group: 1617
Information Disclosure Statement mailed:	February 9, 2004

U.S. PATENT DOCUMENTS

Examiner Initial	Copies Enclosed	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
		4,938,949	07/03/90	Borch			
		5,595,887	01/21/97	Coolidge			
		6,410,058	06/25/02	Gohlke et al.			
		6,500,798	12/31/02	Stanton et al.			
		US 2003/0091606	05/15/03	Stanton et al.			

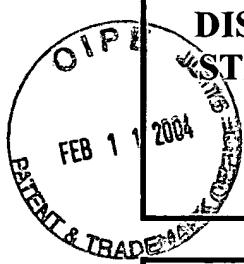
FOREIGN PATENT DOCUMENTS

Examiner Initial	Copies Enclosed	Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	X	WO 95/30686	11/16/95	PCT				
	X	WO 98/14473	04/09/98	PCT				
	X	WO 99/65329	12/23/99	PCT				
	X	WO 00/75173	12/14/00	PCT				
	X	WO 01/11937	02/22/01	PCT				
	X	WO 01/12650	02/22/01	PCT				
	X	WO 01/12651	02/22/01	PCT				
	X	WO 02/13850	02/21/02	PCT				
	X	WO 02/13849	02/21/02	PCT				
	X	WO 02/13851	02/21/02	PCT				
	X	JP 06/041191	02/15/94	Japan (English Abstract Included)				

OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)

EXAMINER	Date Considered
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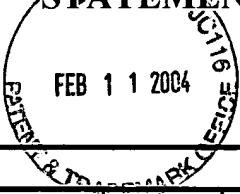
INFORMATION
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STATEMENT

Atty. Docket No.:	265.00390101	Serial No.:	10/691,330
Applicant(s):	Boldogh et al.	Confirmation No.:	1384
Application Filing Date:	October 22, 2003	Group:	1617
Information Disclosure Statement mailed: February <u>9</u> , 2004			

Examiner Initial	Copies Enclosed	Document Description
	X	Altin et al., "Differential Induction of Primary-response (TIS) Genes in PC12 Pheochromocytoma Cells and the Unresponsive Variant PC12nnr5," <i>Journal of Biological Chemistry</i> , 25 March 1991;266(9): 5401-5406.
	X	Anneren et al., "GTK, a Src-related Tyrosine Kinase, Induces Nerve Growth Factor-independent Neurite Outgrowth in PC 12 Cells through Activation of the Rap1 Pathway," <i>Journal of Biological Chemistry</i> , 15 September 2000;275(37): 29153-29161.
	X	Babbit et al., <i>The Vanderbilt Rubber Handbook</i> , R.T. Vanderbilt Company, Inc., Norwalk, CT., 1978: 344-397.
	X	Bagchi et al., "Comparative in vitro and in vivo protein kinase C activation by selected pesticides and transition metal salts," <i>Toxicology Letters</i> , 1997;91: 31-37.
	X	Bespakov et al., "Fabs specific for 8-oxoguanine: control of DNA binding," <i>J Mol Biol.</i> , 1999 Nov 12;293(5): 1085-95.
	X	Bikfalvi et al., "Biological Roles of Fibroblast Growth Factor-2," <i>Endocrine Reviews</i> , February 1997;18(1): 26-45.
	X	Blach-Olszewska et al., "Stimulatory effect of ovine colostrinine (a proline-rich polypeptide) on interferons and tumor necrosis factor production by murine resident peritoneal cells," <i>Ach Immunol Ther Exp (Warsz)</i> , 1997;45(1): 43-47.
	X	"Blast," National Institutes of Health [online] Bethesda, M.D. Retrieved from the Internet on May 14, 2001: <URL: http://www.ncbi.nlm.nih.gov/gorf/b12.html >; 1 pg.
	X	Boldogh et al., "Modulation of 4HNE-Mediated Signaling by proline-rich peptides from Ovine Colostrum," <i>J Mol Neuroscience</i> , May 2003;20(2): 125-134.
	X	Brown et al., "7-Hydroperoxycholesterol and its products in oxidized low density lipoprotein and human atherosclerotic plaque," <i>J. Lipid Res</i> , 1997;38: 1730-1745.
	X	Bruce-Keller et al., "4-Hydroxynonenal, a product of lipid peroxidation, damages cholinergic neurons and impairs visuospatial memory in rats," <i>J Neuropathol Exp Neurol</i> , 1998;57: 257-267.

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Examiner Initial	Copies Enclosed	Document Description
	X	Buescher et al., "Colostral antioxidants: separation and characterization of two activities in human colostrum," <i>J Pediatr Gastroenterol Nutrl.</i> , 1992 Jan;14(1): 47-56.
	X	Buettner, G.R., "The pecking order of free radicals and antioxidants: lipid peroxidation, alpha-tocopherol, and ascorbate," <i>Arch Biochem Biophys</i> , 1993;300: 535-543.
	X	Cadenas et al., "Mitochondrial free radical generation, oxidative stress, and aging," <i>Free Radic Biol Med</i> , 2000;29:222-230.
	X	Calingasan et al., "Protein-bound acrolein: a novel marker of oxidative stress in Alzheimer's disease," <i>J Neurochem</i> . 1999 Feb;72(2):751-6.
	X	Camandola et al., "The lipid peroxidation product 4-hydroxy-2,3-nonenal inhibits constitutive and inducible activity of nuclear factor kappa B in neurons," <i>Brain Res Mol Brain Res</i> , 2000;85:53-60.
	X	Chao "Growth factor signaling: where is the specificity?" <i>Cell</i> . 1992 Mar 20;68(6):995-7.
	X	Chen et al., "Lithium Increase Tyrosine Hydroxylase Levels both In Vivo and In Vitro," <i>Journal of Neurochemistry</i> , 1998;70(4): 1768-1771.
	X	Cheng et al., "Effects on mGST A4 transfection on 4-hydroxynonenal-mediated apoptosis and differentiation of K562 human erythroleukemia cells," <i>Arch Biochem Biophys</i> , 1999;372: 29-36.
	X	Cosgaya et al., "Neuronal differentiation of PC12 cells induced by engrailed homeodomain is DNA-binding specific and independent of MAP kinases," <i>Journal of Cell Science</i> 1998; 111: 2377-2384.
	X	Cui et al., "Effect of Nucleoside Analogs on Neurite Regeneration and Mitochondrial DNA Synthesis in PC-12 Cells," <i>Journal of Pharmacology and Experimental Therapeutics</i> , 1997;280(3): 1228-1234.
	X	Dagø et al., "NS 1231, a novel compound with neurotrophic-like effects <i>in vitro</i> and <i>in vivo</i> ," <i>Journal of Neurochemistry</i> , 2002;81: 17-24.
	X	Davies et al., "Photo-oxidation of proteins and its role in cataractogenesis," <i>J. Photochem. Photobiol B</i> , 2001;63: 114-125.

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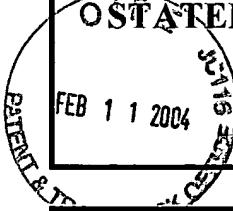
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	X	Davis et al., "Cellular thiols and reactive oxygen species in drug-induced apoptosis," <i>J. Pharmacol Exp Ther</i> , 2001;296: 1-6.
	X	DeJongh et al., "Estimation of Systemic Toxicity of Acrylamide by Integration of <i>in vitro</i> Toxicity Data with Kinetic Simulations," <i>Toxicology and Applied Pharmacology</i> , 1999;158: 261-268.
	X	DeZwart et al., "Biomarkers of free radical damage applications in experimental animals and in humans," <i>Free Radic Biol Med</i> , 1999; 26:202-226.
	X	Doye et al., "Phosphorylation of Stathmin and Other Proteins Related to Nerve Growth Factor-induced Regulation of PC12 Cells," <i>Journal of Biological Chemistry</i> , 15 July 1990;265(20): 11650-11655.
	X	Elgert, "Immunology: Understanding the Immune System," Text (1996) Wiley-Liss 1 st Ed. pp. 24-26 and 199-217.
	X	Esterbauer et al., "Chemistry and biochemistry of 4-hydroxynonenal, malonaldehyde and related aldehydes," <i>Free Radic Biol Med</i> . 1991;11(1):81-128.
	X	Evan et al., "A matter of life and cell death," <i>Science</i> , 1998; 281: 1317-1322.
	X	Feng et al., "NF-κB/Rel Proteins are Required for Neuronal Differentiation of SH-SY5Y Neuroblastoma Cells," <i>Journal of Biological Chemistry</i> , 22 October 1999;274(43): 30341-30344.
	X	Fields et al., <i>Synthetic Peptides: A User's Guide</i> , W.M. Freeman & Company, New York, NY, pp. 77-183 (1992).
	X	Fillmore et al., "Differentiation of PC12 cells with nerve growth factor is associated with induction of transin synthesis and release," <i>J Neurosci Res</i> . 1992 Apr;31(4):662-9.
	X	Finkel et al., "Oxidants, oxidative stress and the biology of ageing," <i>Science</i> , 1998;281: 1317-1322.
	X	Friguet et al., "Protein degradation by the proteasome and its implications in aging," <i>Ann N Y Acad Sci</i> , 2000;908: 143-154.
	X	Gabbita et al., "Increased nuclear DNA oxidation in the brain in Alzheimer's disease," <i>J Neurochem</i> . 1998 Nov;71(5):2034-40.

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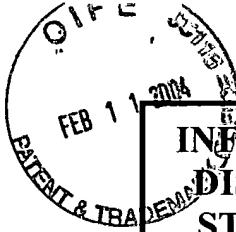
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	X	Gabbita et al., "Decrease in peptide methionine sulfoxide reductase in Alzheimer's disease brain," <i>J Neurochem.</i> 1999 Oct;73(4):1660-6.
	X	Gardner et al., "Development of a peptide antibody specific to human glutathione S-transferase alpha 4-4 (hGSTA4-4) reveals preferential localization in human liver mitochondria," <i>Arch Biochem Biophys.</i> 2001;390: 19-27.
	X	Good et al., "Evidence of neuronal oxidative damage in Alzheimer's disease," <i>Am J Pathol.</i> 1996 Jul;149(1):21-8.
	X	Gratama et al., "Flow cytometric quantitation of immunofluorescence intensity: problems and perspectives. European Working Group on Clinical Cell Analysis," <i>Cytometry.</i> 1998 Oct 1;33(2):166-78.
	X	Grunwald et al., "In situ analysis of chromatin proteins during development and cell differentiation using flow cytometry," <i>Methods Mol Biol.</i> 1999;119:443-54.
	X	Hainut et al., "Redox modulation of p53 conformation and sequence-specific DNA binding in vitro," <i>Cancer Res.</i> 1993;53: 4469-4473.
	X	Han et al., "Implication of a small GTPase Rac1 in the activation of c-Jun-N-terminal kinase and heat shock factor in response to heat shock," <i>J Biol Chem.</i> 2001; 276:1889-1895.
	X	Hensley et al., "Brain regional correspondence between Alzheimer's disease histopathology and biomarkers of protein oxidation," <i>J Neurochem.</i> 1995 Nov; 65(5):2146-56.
	X	Hughes et al., "Modulation of immune responses by anabolic androgenic steroids," <i>Int J Immunopharmacol.</i> 1995 Nov;17(11):857-63.
	X	Hughes et al., "Mediation of nerve growth factor-driven cell cycle arrest in PC12 cells by p53. Simultaneous differentiation and proliferation subsequent to p53 functional inactivation," <i>J Biol Chem.</i> 2000;275: 37829-37837.
	X	Inglot et al., "Colostrinine: a proline-rich polypeptide from ovine colostrum is a modest cytokine inducer in human leukocytes," <i>Arch Immunol Ther Exp (Warsz).</i> 1996;44(4):215-24.
	X	Inglot et al., "Colostrin for treatment of Alzheimer's disease," <i>European Cytokine Network.</i> 1996 Sept;7(3):458(abstract 51).

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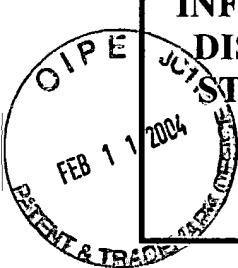

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	X	Inglot et al., "Tumor-associated antigens are cytokine inducers and hyporeactivity factors to the immune system," <i>Biotherapy</i> . 1998;11(1):27-37.
	X	Janusz et al., "Isolation and characterization of a proline-rich polypeptide from ovine colostrum," <i>FEBS Lett.</i> 1974 Dec 15;49(2):276-9.
	X	Janusz et al., "Chemical and physical characterization of a proline-rich polypeptide from sheep colostrum," <i>Biochem J.</i> 1981 Oct 1;199(1):9-15.
	X	Janusz et al., "Proline-rich polypeptide (PRP) - an immunomodulatory peptide from ovine colostrum," <i>Arch Immunol Ther Exp (Warsz)</i> . 1993;41(5-6):275-9.
	X	Kandel et al., "Principles of Neural Science," 4 th Ed.; 2002: 67-81,
	X	Keller et al., "Mitochondrial manganese superoxide dismutase prevents neural apoptosis and reduces ischemic brain injury: suppression of peroxynitrite production, lipid peroxidation, and mitochondrial dysfunction," <i>J Neurosci</i> , 1998;18: 687-697.
	X	Kim et al., "Insulin-like Growth Factor-I-mediated Neurite Outgrowth <i>in Vitro</i> Requires Mitogen-activated Protein Kinase Activation," <i>Journal of Biological Chemistry</i> , 22 August 1997;272(34): 21268-21273.
	X	Kim et al., "Differential Regulation of Insulin Receptor Substrate-2 and Mitogen-Activated Protein Kinase Tyrosine Phosphorylation by Phosphatidylinositol 3-Kinase Inhibitors in SH-SY5Y Human Neuroblastoma Cells," <i>Endocrinology</i> , 1998;139(12): 4881-4889.
	X	Kim et al., "Simultaneous differentiation and quantitation of erythroblasts and white blood cells on a high throughput clinical haematology analyser," <i>Clin Lab Haematol.</i> 1998 Feb;20(1):21-9.
	X	Kimball, John W., "White Blood Cells (leukocytes)," <i>Kimball's Biology Papers</i> [online]. [retrieved on 2002 December 2]. Retrieved from the internet: < http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/B/Blood.html >; 2 pgs.
	X	Kong et al., "Signal transduction events elicited by natural products: a role of MAPK and caspase pathways in homeostatic response and induction of apoptosis," <i>Arch Pharm Res</i> , 2000;23: 1-16.

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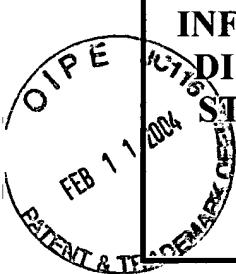


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	X	Kooy et al., "Oxidation of 2',7'-dichlorofluorescin by peroxynitrite," <i>Free Radic Res.</i> 1997 Sep;27(3):245-54.
	X	Kruman et al., "Evidence that 4-hydroxynonenal mediates oxidative stress-induced neuronal apoptosis," <i>J Neurosci</i> , 1997;17:5089-5100.
	X	Kruzel et al., "Towards an Understanding of Biological Role of Colostrinin Peptides," <i>Journal of Molecular Neuroscience</i> , December 2001;17(3): 379-389.
	X	Lachyankar et al., "A Role for Nuclear PTEN in Neuronal Differentiation," <i>Journal of Neuroscience</i> , 15 February 2000;20(4): 1404-1413.
	X	Lafon-Cazal et al., "Nitric oxide, superoxide and peroxynitrite: putative mediators of NMDA-induced cell death in cerebellar granule cells," <i>Neuropharmacology</i> , 1993;32: 1259-1266.
	X	LeBel et al., "Evaluation of the probe 2',7'-dichlorofluorescin as an indicator of reactive oxygen species formation and oxidative stress," <i>Chem Res Toxicol</i> . 1992 Mar-Apr;5(2):227-31.
	X	Leonarduzzi et al., "Lipid oxidation products in cell signaling," <i>Free Radic Biol Med</i> , 2000;28: 1370-1378.
	X	Leszek et al., "Colostrinin: a proline-rich polypeptide (PRP) complex isolated from ovine colostrum for treatment of Alzheimer's disease. A double-blind, placebo-controlled study," <i>Arch Immunol Ther Exp (Warsz)</i> . 1999;47(6):377-85.
	X	Leszek et al., "Colostrinin® proline-rich polypeptide complex from ovine colostrum- a long-term study of its efficacy in Alzheimer's disease," <i>Med Sci Monit.</i> , 2002;8(10): PI93-PI96.
	X	Levi et al., "The mode of action of nerve growth factor in PC12 cells," <i>Mol Neurobiol</i> . 1988 Fall;2(3):201-26.
	X	Ley et al., "Adhesion Molecules in Lymphocyte Trafficking and Colitis," <i>Gastroenterology</i> , October 2001;121(4);Editorial:1008-1010.
	X	Lovell et al., "Elevated thiobarbituric acid-reactive substances and antioxidant enzyme activity in the brain in Alzheimer's disease," <i>Neurology</i> . 1995 Aug; 45(8):1594-601.

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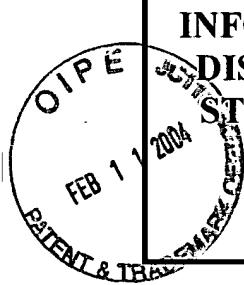

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	X	Lovell et al., "Elevated 4-hydroxynonenal in ventricular fluid in Alzheimer's disease," <i>Neurobiol Aging</i> . 1997 Sep-Oct;18(5):457-61.
	X	Lovell et al., "Decreased glutathione transferase activity in brain and ventricular fluid in Alzheimer's disease," <i>Neurology</i> . 1998 Dec;51(6):1562-6.
	X	Lovell et al., "Increased DNA oxidation and decreased levels of repair products in Alzheimer's disease ventricular CSF," <i>J Neurochem</i> . 1999 Feb;72(2):771-6.
	X	Lovell et al., "Decreased base excision repair and increased helicase activity in Alzheimer's disease brain," <i>Brain Res</i> . 2000 Feb 7;855(1):116-23.
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	X	Markesberry et al., "Four-hydroxynonenal, a product of lipid peroxidation, is increased in the brain in Alzheimer's disease," <i>Neurobiol Aging</i> . 1998 Jan-Feb;19(1):33-6.
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	X	Marshall et al., "Specificity of receptor tyrosine kinase signaling: transient versus sustained extracellular signal-regulated kinase activation," <i>Cell</i> . 1995 Jan 27;80(2):179-85.
	X	Mattson et al., "Alzheimer's disease. Short Precursor shortens memory," <i>Nature</i> , 1997;387: 457-458.
	X	McHeyzer-Williams et al., "Enumeration and characterization of memory cells in the TH compartment," <i>Immunol Rev</i> . 1996 Apr;150:5-21.
	X	Mecocci et al., "Oxidative damage to mitochondrial DNA is increased in Alzheimer's disease," <i>Ann Neurol</i> . 1994 Nov;36(5):747-51.
	X	Mishell et al., <i>Selected Methods in Cellular Immunology</i> , W.H. Freeman, San Francisco, CA; title page and table of contents only, 9 pages (1980).
	X	Montine et al., "Cerebrospinal fluid F2-isoprostane levels are increased in Alzheimer's disease," <i>Ann Neurol</i> . 1998 Sep;44(3):410-3.

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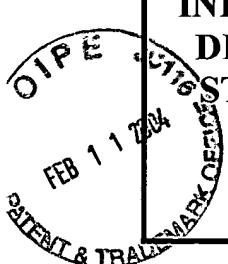


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	Applicant(s): Boldogh et al.	Confirmation No.: 1384
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	X	Nakamura et al., "Redox regulation of cellular activation," <i>Annu Rev Immunol</i> , 1997;15: 351-369.
	X	Ngo et al., "Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox," <i>The Protein Folding Problem and Tertiary Structure Prediction</i> , 1994;14: 491-495.
	X	Noble et al., "Overexpression of Dynamin is Induced by Chronic Stimulation of μ - but Not δ -Opioid Receptors: Relationships with μ -Related Morphine Dependence," <i>Molecular Pharmacology</i> , 2000;58: 159-166.
	X	Ostrea et al., "Influence of breast-feeding on the restoration of the low serum concentration of vitamin E and beta-carotene in the newborn infant," <i>Am J Obstet Gynecol</i> . 1986 May;154(5):1014-7.
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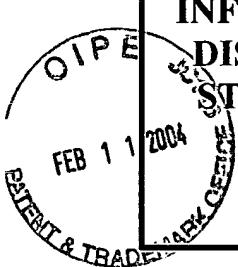

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	X	Ponthan et al., "The Synthetic Retinoid RO 13-6307 induces Neuroblastoma Differentiation <i>in vitro</i> and inhibits Neuroblastoma Tumour growth <i>in vivo</i> ," <i>Int. J. Cancer</i> , 2003;104: 418-424.
	X	Popik et al., "Colostrinin, a polypeptide isolated from early milk, facilitates learning and memory in rats," <i>Pharmacol Biochem Behav</i> . 1999 Sep;64(1):183-9.
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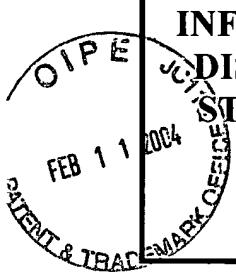


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	X	Salmi et al., "Immune Cell Trafficking in Uterus and Early Life is Dominated by the Mucosal Addressin MadCAM-1 in Humans," <i>Gastroenterology</i> , October 2001;121(4): 853-864.
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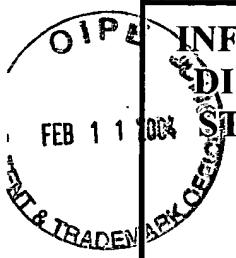


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